REMARKS

The Examiner begins by maintaining her restriction requirement and her position that Group 1 and Group 3 claims cannot be maintained in the same application. It is noted that claims 1, 2 and 3 are under examination. Applicant may file a divisional application for claims 4-9.

Indefiniteness

The Examiner then rejected claims 1-3 as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner suggests the claims are vague and indefinite for use of the term "extract" because this term, in and of itself, does not adequately delineate its metes and bounds. Applicant respectfully traverses the Examiner's position. Extracts are typically defined by the starting material, in this case *Mahonia aquifolium*, and the material used to extract the starting material, or the active ingredient that is contained in the extract. The extraction process of the present invention is described at pages 4 and 5 of the application. The dried bark and twigs are extracted with heat and mixing using water and alcohol as the solvent solution.

As the Examiner suggests the claims are to be interpreted in light of the specification and Applicant argues that the specification provides sufficient guidance with respect to the extract. The specification does indicate that the crude dried *Mahonia aquifolium* is obtained from dried bark and twigs of plants from the *Mahonia aquifolium* family. One of skill in this subject matter would know that other parts of the plant might also be acceptable. The claim has been amended to specify that the extract comprises 1.5 mg of berberine alkaloid per millilitre of extract. Applicant submits that this should be sufficient. Support for the amendment can be found on page 5 of the description.

Anticipation

The Examiner alleges that claims 1 and 2 are anticipated by U.S. Patent No. 5,607,693 to Bonte et al. ("Bonte").

Claim 1 is discussed above as defining a skin treatment composition comprising an extract of *Mahonia aquifolium* in a liposome delivery system.

Claim 2 defines the composition of claim 1, wherein the extract of *Mahonia aquifolium* is present in an amount from 5% to 20% by weight of the total composition.

Bonte describes cosmetic or pharmaceutical compositions containing oxyacanthine, a derivative thereof, a pharmaceutically acceptable salt, or an extract of a plant in which oxyacanthine is present (abstract) (referred to herein as "oxyacanthine"). The concentration of oxyacanthine is between 0.001% and 5%, preferably between 0.01% and 2%, based on the total weight of the composition.

Bonte does not disclose or suggest a skin treatment composition comprising an extract of *Mahonia aquifolium* in a liposome delivery system, wherein the extract comprises 1.5 mg berberine alkaloid/ml extract. In fact, Bonte is silent regarding berberine or its concentration in an extract of *Mahonia aquifolium*. The concentration ranges are also different. Bonte does not disclose a composition wherein the extract of *Mahonia aquifolium* is present in a concentration of from 5% to 20% by weight of the total composition. A concentration of *between 0.001% and 5%* is not equivalent to a concentration *from 5% to 20%*.

There is a very low possibility of an inherent rather than an explicit disclosure. The likelihood that there would be 1.5 mg berberine alkaloid in an extract containing less than 5% oxyacanthine, is very low. This would require the same solubilities and an equal or greater concentration of berberine as compared to oxyacanthine. It would also require selecting Mahonia rather than one of the other plants listed at col. 1, lines 27-30. Note that Mahonia is not included in the list of species at col. 3, lines 52-56. Finally, the extraction process as described at col. 4, lines 46-55, is a plain alcohol extraction. As noted in the Applicant's specification, a simple alcohol extraction does not yield the claimed concentration of berberine alkaloid but a substantially lower concentration, i.e., 0.09 as compared to 1.5 mg/mol. Accordingly, Bonte does not anticipate the claimed composition.

Obviousness

The Examiner alleges that claims 1-3 are obvious over U.S. Patent No. 5,607,693 to Bonte *et al.* ("Bonte") in view of Misik *et al., Planta Med.* 61 372-373 (1995) ("Misik") and Bezakova *et al., Pharmazie*, 51, 758-761 (1996) ("Bezakova").

As discussed above, Bonte does not disclose a skin treatment composition comprising an extract of *Mahonia aquifolium* in a liposome delivery system, wherein the extract comprises 1.5 mg/ml of berberine alkaloid (Claim 1). Bonte does not disclose a composition wherein the extract of *Mahonia aquifolium* is present in a concentration of from 5% to 20% by weight of the total composition (Claim 2). Bonte does not disclose or suggest a composition wherein the extract of *Mahonia aquifolium* is present in a concentration of from 10% by weight of the total composition (Claim 3). Moreover, Bonte does not lead one to prepare an extract from *Mahonia aquifolium* containing 1.5 mg berberine alkaloid/ml extract since Bonte teaches that oxyacanthine is the active ingredient.

Misik evaluates four protoberberine alkaloids (berberine, oxyberberine, jatrorrhizine, columbamine) and two aporphine alkaloids (magnaflorine and corytuberine) for lipoxygenase activity (abstract). The compounds were tested on purified lipoxygenase isolated from sunflower seeds (page 373, second column, 1st paragraph). Misik does not provide the elements missing from Bonte nor does Misik lead one to use a process yielding a many fold higher concentration of berberine alkaloid nor encapsulating it into liposomes.

Bezakova evaluates six bisbenzylisoquinoline (BBIQ) alkaloids: oxyacanthine, armoline, baluchistine, berbamine, obamegine, and aquifoline isolated from *Mahonia aquifolium* for lipoxygenase activity (abstract). Bezakova does not disclose the elements missing from Bonte and Misik nor does Misik lead one to use a process yielding a many fold higher concentration of berberine alkaloid nor encapsulating it into liposomes.

In order to establish a *prima facie* case of obviousness, the references must contain each and every element of the claims. As discussed above, the references, in combination, do not disclose or suggest

> a skin treatment composition comprising
> an extract of *Mahonia aquifolium* comprising 1.5 mg/ml of berberine alkaloid
> in a liposome delivery system.

None of the references discloses or suggests a composition wherein the concentration of the berberine alkaloid is from 5 to 20% and 10%, nor lead one to modify the process described by Bonte to lead to an extract containing at least 1.5 mg berberine alkaloid/ml of extract, respectively. The motivation to combine must come from the references themselves, not the Applicant's disclosure. One of ordinary skill in the art would not be motivated to

combine the references in order to arrive at the claimed compositions, nor is there any disclosure that would lead one of ordinary skill in the art to have a reasonable expectation of success if they did so. Accordingly, the claims, as proposed to be amended, are not obvious over Bonte in view of Misik and Bezakova.

The correction to claim 2 has been made.

Favourable reconsideration and allowance of the present application are respectfully requested.

Respectfully submitted,

Kimberley Lachaine

Kimberley Lachaine
Reg. No. 33,319
Tel. (613) 237-6900
Our File No. 46527
February 14, 2006